

REMARKS

Initially, Applicant would like to thank the Examiner for granting the telephone interview on November 1, 2004, and allowing Applicant to file this supplemental reply to the final Office Action dated August 9, 2004 in view of the Advisory Action dated October 26, 2004.

In the final Office Action, the Examiner maintained the rejection of all pending claims as being obvious over Zhang et al., J. Biol. Chem. 270(15): 8501-8505 ("Zhang") in view of one or both of Miller et al., Biotechniques 7(9): 980-990, 1989 ("Miller") and Jarman et al., Mol. Cell. Bio. 11(9): 4679-4689 ("Jarman"). Independent claim 33 covers a viral expression vector that contains, among others, an enhancer having SEQ ID NO:1 or its complement. Independent claim 51 is drawn to a method of using the expression vector. According to the Examiner, (i) Zhang teaches a non-viral expression vector that has a SEQ ID NO:1-containing HS40 enhancer, (ii) Miller teaches retroviral vectors containing promoters, and (iii) Jarman teaches a regulatory element of the human α globin gene. He proceeded to conclude that it would be obvious to one skilled in the art to combine all of the cited references to make or use the claimed invention.

In the response to the final Office Action, Applicant pointed out that an enhancer, such as that in the Zhang vector, may function in a non-viral vector, but not in a viral vector; and as a result, one skilled in the art would not have been motivated to make a viral vector containing an enhancer in the manner suggested by the Examiner. To support this point, Applicant submitted a copy of McCune with the response. McCune teaches that (1) an enhancer functions well in a non-viral vector, but fails in a viral vector (e.g., a retroviral vector); and (2) viral vector sequences are responsible for the failure. Applicant further rebutted the obviousness rejection by a showing of expected results. More specifically, a viral vector that includes a SEQ ID NO: 1-containing enhancer confers position-independent and copy-number-dependent expression on a transgene. "This was an unexpected result because, previously, transgene expression was limited by position-effect variegation, silencing of transgenes, and the inability to increase expression by increasing the copy number of the specification transgene." See the Specification, page 5, lines 1-5.

Nonetheless, in the Advisory Action, the Examiner did not comment on the just-discussed unexpected results and maintained the rejection on two grounds: First, “claim 33 is not limited to a retroviral vector.” Second, “the response element as taught by McCune is not limited to the ζ -globin enhancer.”

During the above-mentioned interview, Applicant’s counsel proposed amending the independent claims to replace “viral vector” with “retroviral vector.” He also reiterated the unexpected results. The Examiner agreed to the amendment, but requested Applicant to present the unexpected results in a deceleration by the inventor. In addition, he commented on the McCune reference as being limited in scope. Applicant’s counsel stressed that “[the McCune] finding may be applicable to the more general problem of sustaining expression of retrovirus-transduced genes...” (See McCune, page 4477, column 2, lines 12-13) and that the finding contradicted those described in the three cited references. Applicant’s counsel further pointed out that these contradictory teachings in fact indicated the unobviousness of the claimed invention. The Examiner acknowledged the confusion in the art, and requested that Applicant submit an additional relevant paper.

For the purpose of moving this case toward allowance, Applicant has amended the claims at issue agreed by the Examiner and also replied to the Examiner’s two requests:

First, Applicant has amended independent claims 33 and 51 to recite “retroviral vector,” which has necessitated the cancellation of claims 41-44, 47-50, and 58-63, as well as the dependency change to claim 45. Support for the amendment can be found at, e.g., page 1, lines 20-22 of the specification. No new matter has been introduced.

Second, Applicant has submitted a Declaration by Dr. Shen to present the above-discussed unexpected results. More specifically, use of the claimed retroviral vector, but not a control vector, resulted in “position-independent and copy-number-dependent expression on a transgene in an animal.” In addition, the claimed vector drove a continued expression of a transgene into adulthood of the animal, while the control vector failed to do so.

Finally, Applicant has submitted a copy of an additional relevant paper, i.e., Lung et al., *Blood Cells, Molecules, and Diseases*, 2000, 26, 613-619 (“Exhibit A”). This paper teaches a

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Serial No. : 09/977,432
Filed : October 15, 2001
Page : 7 of 7

Attorney's Docket No.: 08919-016003 / 13A-870916
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retroviral vector containing an HS-40 enhancer, N2A γ (HS-40). See, e.g., page 614, FIG. 1. Like the vector described in McCune, the retroviral vector described in this paper failed to drive the expression of a gene operatively linked to the enhancer. See, e.g., page 616, the paragraph bridging columns 1 and 2. In other words, this paper supports the proposition that one skilled in the art would not have been motivated to make and use a retroviral vector containing an enhancer in the manner suggested by the Examiner.

Upon entry of the amendments, claims 33-40, 45, 46, and 51-57 are pending. In view of the above amendments and remarks, as well as the remarks provided in the last response, Applicant submits that amended claims 33 and 51 are not obvious over Zhang in view of Jarman or Miller. The other pending claims all depend from claims 33 and 51 directly or indirectly. They are therefore also not obvious over the cited art.

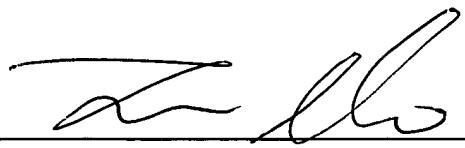
CONCLUSION

Applicant submits that the grounds for the rejection asserted by the Examiner have been overcome, and that claims, as pending, define subject matter that is non-obvious. On this basis, it is submitted that allowance of this application is proper, and early favorable action is solicited.

Please apply any other charges to Deposit Account No. 06-1050, referencing Attorney Docket No. 08919-016003.

Respectfully submitted,

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